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<input type="checkbox"/>	L1	mab near2 96-110	1
<input type="checkbox"/>	L2	hu96-110 or hu-96-110 or (hu near2 96110) or (hu near2 96-110) or ((human or humanized) near2 (96110 or 96-110))	1

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1. [6719971](#). 02 Nov 00; 13 Apr 04. Method for making humanized antibodies. Carter; Paul J., et al. 424/130.1; 424/133.1 424/136.1 424/141.1 424/155.1 435/7.1 530/387.1 530/388.1 530/388.8 530/388.85. A61K039/395.

2. [6713279](#). 04 Feb 00; 30 Mar 04. Non-stochastic generation of genetic vaccines and enzymes. Short; Jay M.. 435/69.1; 435/320.1 435/334 435/6. C12P021/06 C12Q001/68 C12N005/06 C12N015/00.

3. [6703018](#). 28 Feb 01; 09 Mar 04. Method of treatment using humanized anti-CD11a antibodies. Jardieu; Paula M., et al. 424/133.1; 424/141.1 424/143.1 424/144.1 424/152.1 424/153.1 424/193.1 530/387.3 530/388.75 530/391.7. A61K039/395 A61K039/385 C12P021/08 C07K016/34.

4. [6635482](#). 08 Jun 00; 21 Oct 03. Monoclonal antibodies to membrane neutrokinin-.alpha.. Yu; Guo-Liang, et al. 435/326; 435/328 435/331 435/4 530/387.1 530/387.3 530/387.9 530/388.1 530/388.15. C12N005/06 C12Q001/00 C07K016/00 C12P021/08.

5. [6572856](#). 28 Nov 00; 03 Jun 03. Methods for the prevention and treatment of cancer using anti-C3b(i) antibodies. Taylor; Ronald, et al. 424/130.1; 424/133.1 424/136.1 424/138.1 424/141.1 424/143.1 424/152.1 424/174.1 530/387.1 530/387.3 530/387.7 530/388.1 530/388.25 530/391.3 530/391.7. A61K039/395 C07K016/00 C12P021/08.

6. [6569420](#). 30 Jul 01; 27 May 03. Human interferon-.epsilon.: a type I interferon. Chen; Jian, et al. 424/85.4; 424/185.1 424/530 424/85.1 424/85.6 424/85.7 530/351. A61K038/21 A61K045/00 A61K039/00 C07K014/00 C07K019/00.

7. [6468532](#). 20 Jan 99; 22 Oct 02. Methods of treating inflammatory diseases with anti-IL-8 antibody fragment-polymer conjugates. Hsei; Vanessa, et al. 424/145.1; 424/133.1 424/141.1 424/158.1 424/810 530/387.3 530/388.1 530/388.23 530/866 530/868. A61K039/44 A61K039/395 C07K016/24.

8. [6468529](#). 26 Sep 00; 22 Oct 02. Hepatocyte growth factor receptor antagonists and uses thereof. Schwall; Ralph H., et al. 424/130.1; 424/133.1 424/134.1 424/135.1 424/138.1 424/141.1. A61K039/395.

9. [6458355](#). 24 Jul 98; 01 Oct 02. Methods of treating inflammatory disease with anti-IL-8 antibody fragment-polymer conjugates. Hsei; Vanessa, et al. 424/145.1; 424/133.1 424/134.1 424/141.1 424/158.1 424/178.1 424/280.1 530/387.3 530/388.1 530/388.23 530/866. A61K039/44 A61K039/395 C07K016/24.

10. [6429191](#). 30 Mar 01; 06 Aug 02. Treatment of hearing impairments. Gao; Wei-Qiang. 514/2; 514/12 514/192 514/198 514/199. A61K038/00 A61K031/43.

11. [6365156](#). 14 Apr 00; 02 Apr 02. Method for improving the half-life of soluble viral-specific ligands on mucosal membranes. Lee; Peter P.. 424/147.1; 424/159.1 424/163.1 424/164.1 424/196.11. A61K039/40 A61K039/42 A61K039/385.

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□ 12. 6342348. 19 Jan 00; 29 Jan 02. Neurturin receptor. Klein; Robert D., et al. 435/4; 435/7.1 435/7.8 435/7.92 435/7.93 530/350 530/412. C12Q001/00 G01N033/53 C07K001/00 A23J001/00.

□ 13. 6299869. 04 Mar 99; 09 Oct 01. Human interferon-epsilon: a type I interferon. Chen; Jian, et al. 424/85.4; 435/252.33 435/320.1 435/325 435/358 435/69.1 435/69.2 435/69.51 514/12 514/2 530/350 530/351 536/23.1 536/23.52. A61K038/21 A61K038/00 C07K014/00 C07H021/04 C12P021/04.

□ 14. 6264954. 01 Oct 97; 24 Jul 01. Haemophilus outer membrane protein. Chong; Pele, et al. 424/190.1; 424/185.1 424/192.1 424/193.1 424/197.11 424/203.1 424/234.1 424/256.1 435/69.1 435/69.3 435/69.7 530/300 530/350 536/23.7. A61K039/102 C07K014/285 C12N015/31.

□ 15. 6225282. 02 Jan 97; 01 May 01. Treatment of hearing impairments. Gao; Wei-Qiang. 514/2; 514/12 514/192 514/198 514/199. A61K038/00 A61K031/43.

□ 16. 6207152. 17 Feb 98; 27 Mar 01. Hepatocyte growth factor receptor antagonists and uses thereof. Schwall; Ralph H., et al. 424/130.1; 424/133.1 424/138.1 424/141.1 424/143.1 424/152.1 424/155.1 424/156.1 424/174.1 435/7.1 435/7.2 435/7.21 435/7.23 530/387.1 530/387.3 530/388.22 530/388.8 530/388.85 530/389.1 530/389.7. C07K016/18 C07K016/28 A61K039/395.

□ 17. 6200780. 07 Dec 98; 13 Mar 01. Human interferon-.epsilon.(IFN-.epsilon.), a type I interferon. Chen; Jian, et al. 435/69.51; 424/85.4 435/252.3 435/252.33 435/254.2 435/320.1 435/325 435/358 530/351 536/23.52. C12N015/20 C07K014/555 A61K038/21.

□ 18. 6193966. 10 Jul 97; 27 Feb 01. Therapeutic multispecific compounds comprised of anti-Fc.alpha. receptor antibodies. Deo; Yashwant M., et al. 424/136.1; 424/133.1 424/134.1 424/178.1 424/184.1 424/204.1 424/205.1 424/234.1 424/274.1 514/12 514/2 530/387.3 530/388.1 530/395. A61K039/395 C12P021/08 C07K016/28 C07K019/00.

□ 19. 6165466. 14 Aug 98; 26 Dec 00. Antagonists of interleukin-15. Grabstein; Kenneth H., et al. 424/145.1; 424/158.1 424/172.1 424/173.1 530/388.23. A61K039/395 C07K016/00.

□ 20. 6153189. 18 Sep 98; 28 Nov 00. Human TRK receptors and neurotrophic factor inhibitors. Presta; Leonard G., et al. 424/134.1; 424/145.1 514/2 530/300. A61K039/395.

□ 21. 6114147. 17 Nov 97; 05 Sep 00. Immobilized proteins with specific binding capacities and their use in processes and products. Frenken; Leon Gerardus J., et al. 435/69.7; 435/254.11 435/254.2 435/69.8 435/69.9 435/7.1 530/350 536/23.1 536/23.4 536/23.7 536/23.74. C12P021/04 G01N033/53 C12N001/14 C07H021/04.

□ 22. 6080407. 06 Jun 95; 27 Jun 00. Diagnostic assays for MIF. Bucala; Richard J., et al. 424/158.1; 424/145.1 424/198.1 514/169 530/387.3 530/388.23 530/389.2. A61K039/395.

□ 23. 6071725. 02 Dec 97; 06 Jun 00. Vectors expressing ice nucleation protein fusions for cell surface anchoring of foreign proteins. Pan; Jae Gu, et al. 435/69.7; 435/476 435/488 435/69.6 435/69.8 435/71.1 435/71.2. C12N001/21 C12N015/66 C12N015/70 C12P021/02.

□ 24. 6054297. 09 May 95; 25 Apr 00. Humanized antibodies and methods for making them. Carter; Paul J., et al. 435/69.6; 424/130.1 424/133.1 424/138.1 424/155.1 424/174.1 435/328 435/344 435/69.7 530/387.3 530/387.7 530/388.8 530/389.7. A61K039/395 C12N015/13 C07K016/00 C07K016/30.

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□ 25. 6037454. 20 Nov 97; 14 Mar 00. Humanized anti-CD11a antibodies. Jardieu; Paula M., et al. 530/387.3; 435/320.1 530/388.75 530/391.1 530/391.3 530/391.7 536/23.53. C12P021/08 C07H021/04 C12N015/13.

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□ 26. 5925523. 26 Aug 97; 20 Jul 99. Intraction trap assay, reagents and uses thereof. Dove; Simon, et al. 435/6; 435/29. C12Q001/68 C12Q001/02.

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□ 27. 5916558. 22 May 95; 29 Jun 99. Recombinant polypeptides and peptides, nucleic acids coding for the same and use of these polypeptides and peptides in the diagnostic of tuberculosis. Content; Jean, et al. 424/130.1; 424/187.1 435/243 435/320.1 435/325 435/6 435/69.1 435/7.1 435/70.1 435/71.1 530/300 530/350 536/23.1 536/24.1 536/24.3 536/24.31 536/24.32 536/24.33. C07K005/00 G01N033/53 C07H021/04 C12Q001/68.

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□ 28. 5871907. 31 Mar 94; 16 Feb 99. Methods for producing members of specific binding pairs. Winter; Gregory Paul, et al. 435/6; 435/235.1 435/320.1 435/471 435/472 435/476 435/488 435/69.1 435/91.1 435/DIG.47. C12Q001/68 C12P021/02 C12N015/70.

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□ 29. 5866124. 22 May 96; 02 Feb 99. Antiidiotypic antibodies for high molecular weight-melanoma associated antigen. Hardman; Norman, et al. 424/131.1; 424/133.1 435/7.23 435/810 530/387.2 530/387.3. A61K039/395 C07K016/42 C12P021/08 G01N033/574.

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□ 30. 5858657. 07 Jun 95; 12 Jan 99. Methods for producing members of specific binding pairs. Winter; Gregory Paul, et al. 435/6; 435/69.6 435/91.1. C12Q001/68.

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□ 31. 5844092. 20 Dec 94; 01 Dec 98. Human TRK receptors and neurotrophic factor inhibitors. Presta; Leonard G., et al. 530/387.3; 424/133.1 530/350. A61K039/395.

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□ 32. 5837232. 07 Jun 95; 17 Nov 98. Use of an interleukin-10 antagonist to treat a B cell mediated autoimmune disorder. De Waal Malefyt; Rene, et al. 424/85.2; 424/145.1 424/158.1 424/198.1 424/85.1. A61K038/19 A61K039/00.

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□ 33. 5820858. 23 Jan 95; 13 Oct 98. Methods and compositions for inhibiting CD14 mediated cell activation. Leturcq; Didier J., et al. 424/133.1; 424/141.1 424/144.1 424/153.1 435/252.33 435/320.1 435/326 435/328 435/332 435/334 435/343 435/348 435/352 435/363 435/69.6 435/7.21 435/7.9 435/7.93 530/387.3 530/388.22 536/23.53. A61K039/395 G01N033/567 C07K016/00 C07H021/04.

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□ 34. 5770387. 28 Jun 96; 23 Jun 98. Antibodies to mammalian NK antigens and uses. Litwin; Virginia M., et al. 435/7.24; 435/975 530/388.3 530/388.73 530/389.6 530/391.1 530/391.3 530/391.5. C07K016/28 G01N033/577.

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□ 35. 5747035. 14 Apr 95; 05 May 98. Polypeptides with increased half-life for use in treating disorders involving the LFA-1 receptor. Presta; Leonard G., et al. 424/144.1; 424/130.1 424/133.1 424/135.1 424/141.1 424/143.1 424/153.1 424/154.1 424/173.1 514/2 514/8 514/885 530/387.1. A61K039/395 A61K038/02 A61K038/17.

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□ 36. 5665866. 14 Mar 95; 09 Sep 97. Process for obtaining antibodies utilizing heat treatment. Weir; Andrew Neil Charles, et al. 530/390.5; 435/173.8 435/252.3 435/69.6 435/71.1 530/387.1 530/387.3. C12P021/08 C07K016/00 C12N015/13 C12N015/69.

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□ 37. 5223408. 11 Jul 91; 29 Jun 93. Method for making variant secreted proteins with altered

properties. Goeddel; David V., et al. 435/69.3; 435/189 435/195 435/215 435/216 435/226 435/455 435/69.4 435/69.52 435/69.6 435/69.7. C12P021/02 C12N015/62 C12N015/58 C12N015/53.

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<input type="checkbox"/>	L2	fischer.in. and human\$.clm.	86
<input type="checkbox"/>	L3	L2 and (method or process).clm.	58
<input type="checkbox"/>	L4	L3 and bacter\$.clm.	8
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<input type="checkbox"/>	L14	L13 and (antibody or anti-body or antibodies or monoclonal or mono-clonal or scfv or sc-fv or fv or immune or immunoglobulin or igg or igg1 or igg-2 or igg2a or igg-2a or igm or ig or immuno-globulin or globulin).clm.	676
<input type="checkbox"/>	L15	L14 and (treat\$ or prevent\$ or inhibit\$ or infect\$ or bacter\$ or infect\$ or disease or diseases).clm.	383
<input type="checkbox"/>	L16	L15 and (gram near5 positive)	37

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1. 6719971. 02 Nov 00; 13 Apr 04. Method for making humanized antibodies. Carter; Paul J., et al. 424/130.1; 424/133.1 424/136.1 424/141.1 424/155.1 435/7.1 530/387.1 530/388.1 530/388.8 530/388.85. A61K039/395.

2. 6713279. 04 Feb 00; 30 Mar 04. Non-stochastic generation of genetic vaccines and enzymes. Short; Jay M.. 435/69.1; 435/320.1 435/334 435/6. C12P021/06 C12Q001/68 C12N005/06 C12N015/00.

3. 6703018. 28 Feb 01; 09 Mar 04. Method of treatment using humanized anti-CD11a antibodies. Jardieu; Paula M., et al. 424/133.1; 424/141.1 424/143.1 424/144.1 424/152.1 424/153.1 424/193.1 530/387.3 530/388.75 530/391.7. A61K039/395 A61K039/385 C12P021/08 C07K016/34.

4. 6635482. 08 Jun 00; 21 Oct 03. Monoclonal antibodies to membrane neutrokinin-.alpha.. Yu; Guo-Liang, et al. 435/326; 435/328 435/331 435/4 530/387.1 530/387.3 530/387.9 530/388.1 530/388.15. C12N005/06 C12Q001/00 C07K016/00 C12P021/08.

5. 6572856. 28 Nov 00; 03 Jun 03. Methods for the prevention and treatment of cancer using anti-C3b(i) antibodies. Taylor; Ronald, et al. 424/130.1; 424/133.1 424/136.1 424/138.1 424/141.1 424/143.1 424/152.1 424/174.1 530/387.1 530/387.3 530/387.7 530/388.1 530/388.25 530/391.3 530/391.7. A61K039/395 C07K016/00 C12P021/08.

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7. 6468532. 20 Jan 99; 22 Oct 02. Methods of treating inflammatory diseases with anti-IL-8 antibody fragment-polymer conjugates. Hsei; Vanessa, et al. 424/145.1; 424/133.1 424/141.1 424/158.1 424/810 530/387.3 530/388.1 530/388.23 530/866 530/868. A61K039/44 A61K039/395 C07K016/24.

8. 6468529. 26 Sep 00; 22 Oct 02. Hepatocyte growth factor receptor antagonists and uses thereof. Schwall; Ralph H., et al. 424/130.1; 424/133.1 424/134.1 424/135.1 424/138.1 424/141.1. A61K039/395.

9. 6458355. 24 Jul 98; 01 Oct 02. Methods of treating inflammatory disease with anti-IL-8 antibody fragment-polymer conjugates. Hsei; Vanessa, et al. 424/145.1; 424/133.1 424/134.1 424/141.1 424/158.1 424/178.1 424/280.1 530/387.3 530/388.1 530/388.23 530/866. A61K039/44 A61K039/395 C07K016/24.

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32. 5837232. 07 Jun 95; 17 Nov 98. Use of an interleukin-10 antagonist to treat a B cell mediated autoimmune disorder. De Waal Malefyt; Rene, et al. 424/85.2; 424/145.1 424/158.1 424/198.1 424/85.1. A61K038/19 A61K039/00.

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File: USPT

Jun 29, 1993

DOCUMENT-IDENTIFIER: US 5223408 A

TITLE: Method for making variant secreted proteins with altered properties

Detailed Description Text (150):

Suitable host cells for cloning or expressing the vectors herein are the prokaryote, yeast, or higher eukaryote cells described above. Suitable prokaryotes include eubacteria, such as Gram-negative or Gram-positive organisms, for example, *E. coli*, *Bacilli* such as *B. subtilis*, *Pseudomonas* species such as *P. aeruginosa*, *Salmonella typhimurium*, or *Serratia marcescans*. One preferred *E. coli* cloning host is *E. coli* 294 (ATCC 31,446), although other strains such as *E. coli* B, *E. coli* 1776 (ATCC 31,537), and *E. coli* W3110 (ATCC 27,325) are suitable. These examples are illustrative rather than limiting. Preferably the host cell should secrete minimal amounts of proteolytic enzymes. Alternatively, in vitro methods of cloning, e.g. PCR or other nucleic acid polymerase reactions, are suitable.

## CLAIMS:

1. A method for making a variant secretory protein retaining at least one desired binding property and eliminating at least one undesired binding property of the wild-type secretory protein comprising:
  - (a) mutating the DNA encoding the selected wild-type protein thereby creating a library of related variant DNA molecules;
  - (b) inserting each DNA molecule created in step (a) into an expression vector, wherein the vector comprises DNA encoding a transmembrane anchor domain thereby creating a library of vectors;
  - (c) transfecting eukaryotic cells with the vectors of step (b);
  - (d) culturing the cells of step (c) under conditions inducing the expression of the DNA to produce a chimeric fusion protein immobilized on the cell membrane;
  - (e) contacting the cultured cells of step (d) with first and second reporter molecules capable of binding to different epitopes on the wild-type protein, each reporter molecule containing a fluorophore different from the fluorophore of the other reporter molecule, with said contacting taking place under conditions for which at least a portion of the cultured cells bind to the first or second reporter molecules;
  - (f) sorting the contacted cells based on a desired binding pattern with the first or second reporter molecules; and
  - (g) obtaining the variant proteins having the desired binding pattern from the sorted cells from (f).
2. The method of claim 1 wherein step (g) comprises isolating the variant protein from the sorted cells.
3. The method of claim 1 wherein step (g) comprises isolating the variant DNA

molecule and producing the variant protein from the isolated variant DNA molecule by by recombinant methods.

4. The method of claim 1 wherein step (g) comprises sequencing the variant DNA molecule, determining the codons encoding amino acids in the variant protein that produce the desired binding pattern, altering those codons in a DNA molecule encoding the wild-type protein, and producing the variant protein from the DNA containing the altered codons by recombinant methods.

5. The method of claim 1 wherein the first and second reporter molecules comprise a detectable marker conjugated to a molecule selected from the group; antibodies, ligands, and soluble receptors.

6. The method of claim 5 wherein the first and second reporter molecules comprise a first and a second monoclonal antibody (Mab) each conjugated to a different fluorophore.

7. The method of claim 6 wherein the sorting step comprises fluorescence activated cell sorting (FACS).

8. The method of claim 1 wherein the DNA encoding the transmembrane anchor domain encodes the membrane glycoprophospholipid anchor sequence of decay acceleration factor (DAF).

9. The method of claim 8 wherein the selected wild-type protein is selected from the group; growth hormone, human growth hormone (hGH), des-N-methionyl human growth hormone, bovine growth hormone, parathyroid hormone, thyroxine, insulin A-chain, insulin B-chain, proinsulin, relaxin A-chain, relaxin B-chain, prorelaxin, follicle stimulating hormone (FSH), thyroid stimulating hormone (TSH), leutinizing hormone (LH), glycoprotein hormone receptors, calcitonin, glucagon, factor VIII, an antibody, lung surfactant, urokinase, streptokinase, human tissue-type plasminogen activator (t-PA), bombesin, factor IX, thrombin, hemopoietic growth factor, tumor necrosis factor-alpha and -beta, enkephalinase, human serum albumin, mullerian-inhibiting substance, mouse gonadotropin-associated peptide, .beta.-lactamase, tissue factor protein, inhibin, activin, vascular endothelial growth factor, integrin receptors, thrombopoietin, protein A or D, rheumatoid factors, NGF-.beta., platelet-growth factor, transforming growth factor; TGF-alpha and TGF-beta, insulin-like growth factor-I and -II, insulin-like growth factor binding proteins, CD-4, DNase, latency associated peptide, erythropoietin, osteoinductive factors, interferon alpha, -beta, and -gamma, colony stimulating factors (CSFs), M-CSF, GM-CSF, and G-CSF, interleukins (ILs), IL-1, IL-2, IL-3, IL-4, IL-6, IL-7, superoxide dismutase; viral antigens, HIV envelope proteins GP120 and GP140, immuno globulins, and fragments of the above-listed proteins.

10. The method of claim 9 wherein the protein is a human protein.

11. The method of claim 1 wherein the eukaryotic cell is a mammalian cell.

12. The method of claim 1 wherein the desired binding pattern comprises binding of the cells with the first reporter molecule and the absence of binding of the cells with the second reporter molecule.

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Oct 14, 2003

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TITLE: Directed human immune globulin for the prevention and treatment of staphylococcal infections

INVENTOR (1):

Fischer; Gerald W.

Other Reference Publication (7):Timmermann et al., Characterisation and Functional Aspects of Monoclonal Antibodies Specific for Surface Proteins of Coagulase-Negative Staphylococci, J. Med. Microbiol., vol. 35, pp. 65-71 (1991).Other Reference Publication (9):Ichiman et al., "Monoclonal IgM Antibody Protection in Mice Against Infection with an Encapsulated Strain of Staphylococcus epidermidis," Can. J. Microbiol., 37:404-407 (1991).